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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/601,667	10/06/2000	Peter Morris	29841/36636	9526

7590 04/09/2003

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EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1653	18

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/601,667	Applicant(s) MORRIS ET AL.	
	Examiner Samuel W Liu	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08/03/02, 03/1902, 08/29/02 and 03/14/03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-90* is/are pending in the application.

4a) Of the above claim(s) *46-48,55-77 and 81-90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-54 and 78-80* is/are rejected.

7)☒ Claim(s) *50* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' preamendment filed 3 August 2002 (Paper No. 6) as to amendment of claims 17, 24, 26, 29,33, 36, 36-37 and 44, amendment filed 19 March 2002 (Paper No. 9) as to cancellation of claims 1-45 and addition of claims 46-90 (Paper No. 9), and amendment filed 29 August 2002 (Paper No. 10) as to amendment of claims 46-51 and 85-87 have been entered. Also, applicants' requests for extension of time of one month filed 19 March 2002 (Paper No. 8) and for one month filed 29 August 2002 (Paper No. 14) have been entered. The following is applicable to the pending claims 8-14.

Foreign Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119 (a)-(d) based on an application filed in Germany (19804210.8) on February 3, 1998.

Election/Restrictions

Applicant's election of Group II, claims 49-54 and 78-80 with traverse (filed 14 March 2003, Paper No. 17) is acknowledged. The traversal is on the ground that all claims is linked by a single general inventive concept. The Applicant's traversal has been considered. But it is unpersuasive.

The inventions listed as Groups I-IX do not related to a single general invention concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features are known in the art. See the rejections for anticipation. Thus, the products lack special technical feature linking all claims, as defined by PCT Rule 13.2 and 37 CFR 1.475(a), as a single contribution over the art, and a holding of lack of unity is therefore proper,

i.e., the restriction requirement under 35 U.S.C. 121 and 372 which is mailed 11 February 2003 is deemed proper.

Thus, the pending claims 46-48, 55-77 and 81-90 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected inventions. Claims 49-54 and 78-80 are examined in this Office action.

Objection to claims /specification

In claim 50 "MLA" should be spelled out for the first time instance of use in the claims

In page 4, lines "SDS-PAGE" should be spelled out for the first instance of use. See also page 4, line 20, "HPLC"; page 12, line 5, "PCR"; and page 13, line 4, "RACE".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 49-54 and 78-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 49 is indefinite in the recitation "or a fragment thereof"; does said fragment include the limitation "Xaa at position 533 of SEQ ID NO:1" or the limitation "Xaa at position 534 of SEQ ID NO:1"? which one is it. In addition, the recitation "a fragment" is unclear as to whether or not the said fragment is derived from (i) he sequence of SEQ ID NO:1, or (ii) from

the sequence of SEQ ID NO:40, or (iii) from the fusion polypeptide chain comprising both SEQ ID NOs: 1 and 40? The dependent claims are also rejected.

Claim 78 is indefinite with regard to "and/or" because the it not apparent as to whether or not the claimed pharmaceutical composition comprises both the polypeptide of claim 49 and a fragment thereof, or comprises only the polypeptide of claim 49 or only a fragment of the polypeptide.

Claim 80 contains an inappropriate Markush-type wording in the claim, *i.e.*, the term "comprising", which should be changed to the closed language "consisting of" because the group needs to be a "closed" group, whereas "comprising" is open ended.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 49-54 and 78-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of the full-length polypeptide sequences of SEQ ID NOs:1, 4, 40 and 41. Applicant has not described any structural variants of the full-length sequences of SEQ ID NOs: 1, 4, 40 and 41; or any the amino acid sequences, i.e., fragments, that are only a

portion (as short as comprising only 3 amino acid residues, for example) of the full-length of the sequences.

The current claim language encompasses a large number of the polypeptide variants (fragments) that are deviated both structurally and functionally from the claimed amino acid sequences consisting of SEQ ID NOs: 1-4, 6-11, 38 and 40-41. The specification provides insufficient teaching, guidance, and no working examples of these variant molecules as claimed. (see claims 78-80).

The specification does not provide experimental evidence of an animal model to demonstrate using the claimed polypeptides as the pharmaceutical composition neither does relevant animal model for the polypeptide fragments (variants); This issue is with regard to whether or not the claimed composition would function as pharmaceutical composition. In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the pharmaceutical composition as claimed, and absence of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical composition are effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success. Thus, applicants are not in possession of the pharmaceutical composition comprising the polypeptides fragments (variants).

Applicant has disclosed only the polypeptides of SEQ ID NOs: 1-4, 6-11, 38 and 40-41; therefore, the skilled artisan would not have envisioned all the contemplated sequence possibilities recited in the instant claims in term of "fragments". Consequently, conception is achieved until a representative description of the structural and functional properties of the

claimed invention, *i.e.*, the fragment, has occurred, regardless of the complexity or simplicity of the method of making the polypeptides. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993).

The current claim language of " a fragment thereof " broadly encompasses a variety of both genetic mutants (*i.e.*, naturally-occurring variants), *e.g.*, RNA-editing and mRNA-splicing products which are result from genetic deletion, insertion and sequence exchanging event (see page 5, lines 1-7), and human-generated (*i.e.*, recombinant) mutations (see page 13, the fourth paragraph) including chemical modification, *e.g.*, glycosylation, (see page 29, lines 3-12). Applicants therefore are not possession of having all fragments that is structurally deviated from the disclosed polypeptide sequences stated *supra*, and all types of mutations generated either genetically or recombinantly. Without characterization each polypeptide or peptide variant, the variant or fragment thereof is unpredictable in view of structure and function.

A description of the reduction to practice of the invention, unaccompanied by any meaningful, distinguishing characteristics the polypeptide variants and use of the mutants or variants is insufficient to satisfy the written description requirement of 35 U.S.C. §112. The inventors have not provided any description of the variant(s) of SEQ ID NOs: 1, 4, 40 and 41 polypeptides.

The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, the first paragraph "Written Description" Requirement make clear that the written description requirement for a claimed invention may be satisfied through sufficient description of a representative examples with relevant, identifying characteristics, *i.e.*, structure or other physical

and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that the applicants were in possession of the invention (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

One of skill in the art would reasonably have concluded that the disclosure fails to provide a representative number of the polypeptide fragments or variants, which are recombinantly or/and genetically produced, to describe its use in binding of the cellular recognition molecule. The application, therefore, does not show possession of the claimed peptide variants (fragments) or sub-sequences of the SEQ ID NOs: 1-4, 6-11, 38 and 40-41 and use of the same to prepare the claimed pharmaceutical composition thereof. *See University of California v. Eli Lilly and co. 43 USPQ2d 1398.*

Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 49-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Soler, M. H. et al. (*FEBS Lett.* (1996) 399, 153-157).

Soler et al. teach the amino acid sequence (see Figure 2) comprising the sequence from residue 1 to residue 62) that reads on the fragments of SEQ ID NOs: 1, 2 and 40 (residues 1- 62) of the current application. Because the claims set forth that a mistletoe lectin polypeptide comprising a fragment of the sequences comprising SEQ ID NOs; 1 and 40 thereof, wherein "a fragment" is an open-ended language, and because the claims do not make it clear that as to whether or not the claimed fragment includes "Xaa at position 533" of SEQ ID NO:1" or the "Xaa at position 534 of SEQ ID NO:1" (see also the rejection under 35 USC 112, the second paragraph), the Soler et al. reference anticipates claims 49-51 of the instant application.

Claims 49-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Sweeney, R. A. P. et al. (*J. Mol. Biol.* (1993)234,1279-1281). Sweeney et al. teach A chain and B chain of

Mistletoe lectin (*Viscum Album*) polypeptides (se page 1280) which are the same molecules of the current disclosure and possess the sequence identity of at least more than tow amino acid residues in view of the molecular inherence and homology of the same type of Mistletoe lectin derived polypeptides. Because the current claim language "a fragment" is open-ended and indefinite as to whether or not the said fragment includes "Xaa at position 533" or the "Xaa at position 534 of SEQ ID NO:1" (see also the rejection under 35 USC 112, the second paragraph), the Sweeney et al. reference is applied to claims 49-51 of the current application.

Claims 49-51 and 78-80 are rejected under 35 U.S.C. 102(e) as being anticipated by Lentzen, H. et al. (US Pat. No. 6271368).

Lentzen et al. teach a polypeptide sequence of SEQ ID NO:35 (columns 49-52) comprising a fragment (amino acid residues 49 – 95) that reads on the sequence of SEQ ID NOs: 1, 2 and 40 (amino acid residues 16 – 62) of the instant application, and teach a polypeptide sequence of SEQ ID NO:43 (columns 55-58) comprising a fragment (amino acid residues 19 – 89) that reads on the sequence of SEQ ID NOs: 1 and 2 (amino acid residues 19 – 89) of the instant application. Because the current claim language "a fragment" is open-ended and indefinite as to whether or not the said fragment includes "Xaa at position 533" or the "Xaa at position 534 of SEQ ID NO:1" (see also the rejection under 35 USC 112, the second paragraph), the Lentzen et al. patent anticipates claims 49-51 of the instant application.

Since Lentzen patent teach a pharmaceutical composition comprising the said mistletoe lectin polypeptide sequences (see claims 1, 22, and 28-29), claim 78 is anticipated by the Lentzen patent as well.

Further, Lentzen et al. teach therapeutic composition, *i.e.*, combination preparation (see column 13, lines 3-30), comprising the mistletoe lectin (ML) polypeptide stated above and a cell receptor ligand that is colony-stimulating factors (note that colony-stimulating factors include granulocyte colony-stimulating factors also called G-CSF which is a type of cell membrane receptor). The Lentzen et al. teaching thus meets the limitation set forth in claims 79-80 of the current application.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483. The examiner can normally be reached from 9:00 a.m. to 5:30 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 703-308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

Samuel Wei Liu, Ph.D.

March 31, 2003

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